REMARKS

Status

By this Amendment, new claims 41-43 are added; claim 26 is canceled; claims 23, 24, 25, 27, 29, 34, 36 and 38 are amended to more clearly define the claimed subject matter and to correct the spelling of certain terms ("semicarbazide" and "aminooxy") and other typographical errors. Support for the new claims and amendments is present in the specification as filed at least at, e.g., page 8, lines 12 to page 9, line 8; page 9, lines 14-17; page 12, line 23 to page 13, line 19; page 15, lines 18-28, original claims; and Figure 1. No new matter is added.

Interview of May 6, 2005

Applicant thanks Examiner Khare for conducting the interview. At the interview, amendments to claims and arguments as now presented were discussed with the Examiner. An agreement was reached that such amendments and arguments would be sufficient to overcome the outstanding rejections.

35 U.S.C. § 112

The Examiner previously rejected claims 23-40 under § 112, ¶2, as not sufficiently specific with respect to the terms "an oligosaccharide containing a phosphorylated hexose" and "a compound containing a carbonyl-reactive group". Applicant has now amended claims to define the oligosaccharide as "an oligosaccharide containing a phosphorylated mannose". Applicant has also replaced the second term with the wording "to generate a carbonyl-reactive group". Examiner Khare indicated at the interview that these amendments warrant withdrawal of the § 112 rejection.

35 U.S.C. § 103

Claims 23-40 have been rejected as allegedly being obvious over Tolvanen et al. (1986) J. Biol. Chem. 261(20):9546-9551 ("*Tolvanen*") in combination with U.S. Patent No. 6,251,858 ("*Monsigny*"). The Examiner argued that *Tolvanen* teaches the use of hydrazine derivatives to attach oligosaccharides to miscellaneous cell surface glycocoproteins. The Examiner further argued that *Monsigny* supplements *Tolvanen* by showing coupling of biantennary or triantennary mannopyranosyl oligosaccharides containing mannose-6-phosphate to a protein (1/12/05 Office Action at pages 4 and 5). Based on these references, the Examiner suggests that it would have been obvious to use the hydrazine derivatives of *Tolvanen* for coupling mannose-6-phosphate containing oligosaccharides of *Monsigny* to lysosomal enzymes. Applicant respectfully disagrees.

A *prima facie* case of obviousness requires that all the claim limitations must be taught or suggested by the cited references. M.P.E.P. § 2142. A *prima facie* case of obviousness further requires a teaching or a suggestion to make the claimed combination and a reasonable expectation of success, all of which must be found in the prior art, and not in applicant's disclosure. Impermissible hindsight must be avoided. *Id.*

First, contrary to the articulated requirements, neither *Tolvanen* nor *Monsigny* contains any mention of any lysosomal enzymes. For at least this reason, the *prima facie* case is not proper.

Second, the cited references lack the requisite suggestion or motivation and to use *Tolvanen's* method on lysosomal enzymes. The Examiner has previously acknowledged that *Tolvanen* differs from Applicant's invention in that it does not

suggest coupling of a phosphorylated oligosaccharide to a glycoprotein such as a lysosomal enzyme (4/16/04 Office Action at page 5). Indeed, glycoproteins illustrated by *Tolvanen* are dissimilar to lysosomal enzymes. *Tolvanen* uses an assortment of glycoproteins on the cell surface of red blood cells and K562 cells. The lysosomal enzymes, on the other hand, are a group of enzymes specific to the lysosome, an intracellular organelle. They are unique in their localization and function in the cell.

The Examiner has also previously acknowledged that *Monsigny* does not suggest a method of coupling an oxidized glycoprotein with a derivatized phosphorylated mannopyranosyl oligosaccharide (4/16/04 Office Action at page 6). Given that *Tolvanen* nor *Monsigny* do not mention or suggest lysosomal enzymes, these references fail to provide a suggestion or motivation required for a *prima facie* case of obviousness.

Third, *Tolvanen* and *Monsigny* do not provide a reasonable expectation of success. *Tolvanen* provides no information on biological, or enzymatic, activity of proteins after oxidation and conjugation. None of the proteins actually tested by *Tolvanen* are purified enzymes, much less lysosomal enzymes. *Monsigny* does not cure the defects of *Tolvanen*. *Monsigny* merely lists phosphorylated oligosaccharides as one of many existing types of oligosaccharides.

Therefore, claims 23-25, 26-43 are not obvious over *Tolvanen* and *Monsigny*, alone or in combination.

PATENT
Customer No. 22,852
Attorney Docket No. 07680.0031-00000

Conclusion

In view of the above amendments and arguments, all pending claims are believed to be allowable. The Examiner is invited to call the undersigned with any questions or concerns.

Respectfully submitted,

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Dated: May 11, 2005

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